ATTACHMENT II - New Claims 59-116

59. A pharmaceutical composition for the treatment of the risk f actors of syndrome X of Reaven comprising as active ingredient a compound selected among somatostatin or one of its analogs (as herein defined) , diazoxide or one of its analogs (as herein defined), cyclothiazideor one of its analogs(as herein defined) and metformin.

60. The pharmaceutical according to claim 59 further comprising an additional Compound.

61. The pharmaceutical composition according to claim 59 comprising an additional compound having an additional pharmaceutical effect.

62. A pharmaceutical composition according to Claim 60 wherein the additional compound is selected among carriers, solvents and emulgamators.

63. A pharmaceutical composition according to Claim 59, wherein the analog of somatostatin is Octreotide.

64. A pharmaceutical composition according to Claims 59, wherein the analog of somatostatin is Vapreotide.

65. A pharmaceutical composition according to Claim 59, wherein the analog of somatostatin is Lanreotide.

66. A pharmaceutical composition according to Claim 59, wherein the analogs of somatostatin are Cyclopeptide somatostatin analogues selected among

Cyclo(Pro-Phe-D-Trp-Lys-Thr-Phe]

Cyclo[N-Me-Ala-Tyr-D-Trp-Lys-Val-Phe

Cyclo[Pro-Ala-D-Trp-Lys-Thr-Phe]

Cyclo[Pro-Tyr-D-Trp-Lys-Thr-Phe]

Cyclo[Pro-Phe-D-Trp-Lys-α-aminobutyric-Phe]

Cyclo[N-Me-Ala-Phe-D-Trp-Lys-Thr-Phe]

Cyclo[Pro-Phe-D-Trp-Lys-Val-Phe]

Cyclo[D-Ala-D-Phe-D-Trp-L-Lys-D-Thr-N-Me-D-Phe]

Cyclo(Pro-Phe-D-Trp-Lys-Thr(Bzl)] (Bzl =(a)

Cyclo[Pro-Phe-D-Trp-Lys-Thr-Phe]

Cyclo[Pro-D-Phe-D-Trp-Lys-Thr(Bzl)

Cyclo(Ahep-Lys-Asn-Phe-Phe-Trp-Lys-Thr-

Tyr-Thr-Ser] [SEQ ID NO 1] (Ahep =(b)

Cyclo[Ahep-Phe-D-Trp-Lys-Thr(Bzl)]

Cyclo(Ahep-Phe-D-Trp-Lys-Thr]

Cyclo(Ahep-Phe-D-Trp-Lys-Ser(Bzl)

Cyclo [Ahex-Phe-D-Trp-Lys-Thr (Bzl) (Ahex = (c)

Cyclo[Aoct-Phe-D-Trp-Lys-Thr(Bzl)) (Aoct = (d)

Cyclo(Ala-Cys-Phe-D-Trp-Lys-Thr-Cys]

(a) Bzl = benzyl

(b) Ahep = 7-aminoheptanoyl

(c) Ahex = 6-aminohexanoyl

(d) Aoct = 8-amino-octanoyl.

67. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Phe-[Cys-Phe-D-Trp-Lys-Thr-cys]-Thr-ol

68. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Nal-[Cys-Tyr-D-Trp-Lys-Val-Cys]-Thr-NH_2 (Nal = (1)

69. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Phe- [Cys-Tyr-D-Trp-Lys-Val-Cys] -Nal-NH_2

70. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Phe- [Cys-Tyr-D-Trp-Lys-Thr-Cys] -Nal-NH_2

71. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Phe- [Cys-Tyr-D-Trp-Lys-Abu-Cys]-Nal-NH_2 (Abu = (2)

72. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Phe-[Cys-Tyr-D-Trp-Lys-Ser-Cys)-Nal-NH_2

73. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Nal-[Cys-Tyr-D-Trp-Lys-Val-Cys] -Nal-NH_2

74. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

c (Ahep-Trp-D-Trp-Lys-Thr-Phe) (Ahep, = (3)

75. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Phe-Cpa-Tyr-D-Trp-Lys-Thr-Phe-Thr-NH_2 (Cpa = (4)

76. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Phe-Cpa-Tyr-D-Trp-Lys-Val-Phe-Thr-NH_2

77. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH_2

78. A pharmaceutical composition according to Claim 59 wherein the somatostatin analog is:

D-Phe-Phe-Phe-D-Trp-Lys-Val-Phe-Thr-NH_2

79. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Phe-Phe-Tyr-D-Trp-Lys-Val-Phe-D-Nal-NH_2

80. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Phe-Ala-Phe-D-Trp-Lys-Ala-Nal-NH_2

81. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Phe-Phe-Phe-D-Trp-Lys-Val-Phe-Thr-NH_2

82. A pharmaceutical composition according to Claim 59, wherein the- somatostatin analog is:

D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH_2

83. A pharmaceutical composition according to Claim 59, wherein the. somatostatin analog is:

D-Phe-Phe-Tyr-D-Trp-Lys-Val-Phe-D-Nal-NH_2

84. A pharmaceutical composition according to Claim 59, wherein the somatostatin analogs are polypeptides of the formula:

X-Lys-Asn-Phe-Phe-A-Lys-Thr-Phe-Thr-Ser-Y

wherein A is L- or D-Trp,

X is H-$(Aeg)_m$-Cys- or H-$(Aeg)_m$-Ala-Gly-Cys-,

Y is -Cys- $(Aeg)_n$-OH or

X and Y taken together are a 2 -amino ethy 1-glycyl group in the ring position and

m and n are 0, 1, 2, provided that

m and n are at least 1,

and their cyclic disulfide derivatives.

85. A pharmaceutical composition according to Claim 59, wherein the somatostatin analogs are peptides of the formula:

Bmp-Lys-X-Phe-Phe-trp-Lys-Thr-Phe-Thr-Y-Cys-OH

3 4 5 6 7 8 9 10 11 12 13 14 [SEQ ID NO 2]

in which

Bmp represents the desaminocysteine radical,

X represents Asn,

trp represents D-Trp that may be substituted in the benzene ring by a halogen atom, and

Y represents the radical of an alpha-(lower alkyl) amino- (lower alkyl)-carboxylic acid having a minimum of 4 and a -maxinum of 8

carbon atoms, in which the two lower alkyl radicals can be connected to one another with a single C-C bond, an oxygen atom or a sulphur (II) atom.

86. A pharmaceutical composition according to Claim 59, wherein the somatostatin analogs are cyclic octapeptides of the formula:

Asn-Phe-Phe-Trp-Lys-Thr-Phe-Gaba(Ar) [SEQ ID NO 3]

5 6 7 8 9 10 11 12

in which

Trp represents L-Trp or D-Trp, in which the benzene ring may be substituted by a fluorine a tam, and

Gaba(Ar) represents the residue of a α-aminobutyric acid substituted by a cyclic hydrocarbyl radical Ar selected from the group consisting of cyclohexyl; phenyl optionally substituted by halogen, nitro or phenoxy; and naphthyl optionally substituted by halogen.

87. A pharmaceutical composition according to Claim 59, wherein the somatostatin analogs are compounds of formula

H-Ser-Ala-Asn-Ser-Asn-Pro-Ala-R_8-Ala-Pro-Arg-Glu-Arg-Lys-Ala-Gly-Cys-R_{18}-R_{19}-Phe-Phe-D

-Trp-Lys-Thr-R_{25}-R_{26}-R_{27}-R_{28}-OH wherein R_8 is Met or Leu, R_{18} is Lys or des R_{18}, R_{19} is Asn or des R_{19}, R_{25} is Phe or Tyr, R_{26} is Thr or des R_{26}, R_{27} is Ser or D-Ser and R_{28} is D-Cys or Cys.

88. A pharmaceutical composition according to Claim 59, wherein the somatostatin analogs are compounds of formula

H-Ser-Ala-Asn-Ser-Asn-Pro-Ala-R_8-Ala-Pro

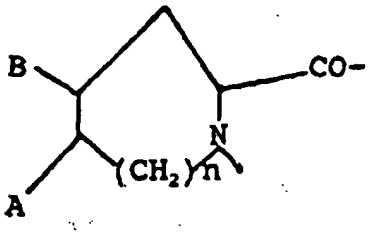
-Arg-Glu-Arg-Lys-Ala-Gly-Cys-R_{18}-R_{19}-Phe-Phe-D-Trp-Lys

-Thr-R_{25}-R_{26}-R_{27}-R_{28}-OH wherein R_8 is Met or Leu, R_{18} is Lys or des R_{18}, R_{19} is Asn or ~~des R_{19}, R_{25}~~ is Phe or Tyr, R_{26} is Thr or des R_{26}, R_{27} is Ser or D-Ser and R_{28} is D-Cys or Cys, or the linear version thereof where the disulfide bridge is replaced by hydrogen.

89. A pharmaceutical composition according to Claim 59, wherein the somatostatin analogs are cyclic hexapeptides of the formula

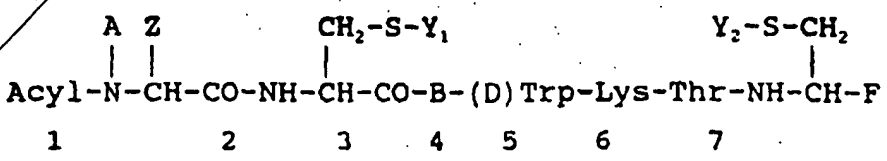
-X - Phe-D-Trp-Lys-Y-Phe

in which X represents the radical of an L-amino acid of the formula



in which A and B are identical or different and denote alkyl having 1 to 3 carbon atoms, or A and B together represent a saturated, unsaturated or aromatic monocyclic or bicyclic structure having 3 to 6 carbon atoms, n denotes 0 or 1, and Y represents an aliphatic or aromatic L-amino acid the side-chair of which can be hydroxylated, said amino acid being selected from the group consisting of L-alanine, L-serine, L-valine, L-leucine, L-isoleucine, L-phenylalanine and L-tyrosine.

90. A pharmaceutical composition according to Claim 59, wherein the somatostatin analogs are N-acyl-polypeptides of formula,



wherein "Acyl" is a group of formula R^1CO- wherein R^1 is C_{1-20}, alkyl or phenyl; a group-of formula $R^{11}SO_2$- wherein R^{11} is C_{1-20} - alkyl, phenyl or tolyl; a group

wherein

R^{III} and R^{IV} are each independently hydrogen

or C_{1-10} alkyl; or biotinyl,

A is hydrogen or C_{1-3} alkyl,

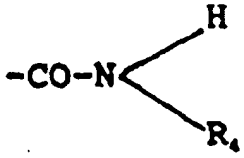
>N-CH(Z)-CO- is an (L)- or (D)-phenylalanine residue optionally ring-substituted by NO_2 or an (L) or (D) -norleucine residue,

whereby

Z in >N-CH(Z)-CO- represents the remainder of said residue,

B is -Phe- optionally ring-substituted by NO_2,

F is a group of formula



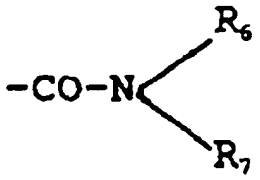
wherein R, is hydrogen or a group of formula

$-CH(R_5)-X$,

R_5 is $CH_3CH(OH)-$, i-butyl or benzyl

X is a group of formula $-COOR_1$,

$-CH_2OR_2$ or



wherein R_1, R_6 and R_7, are each hydrogen or

C_{1-3} alkyl, and

R_2 is hydrogen or the residue of a

physiologically acceptable,

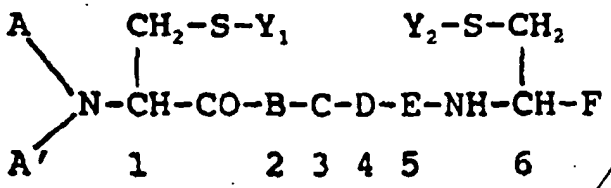
physiologically hydrolysable

ester,

the group $-CH(R_5)-X$ having the (D)- or (L)-configuration and Y_1, and Y_2 are each hydrogen or together represent a direct bond, whereby the residue resides in the 2- and 7-position each independently have the (L)- or (D)-configuration, and with the proviso that:

i) (L)- and/or (D)-cysteine residues are present at the 2- and 7-positions only.

91. A pharmaceutical composition according to Claim 59, wherein the somatostatin analogs are polypeptides of the formula



wherein A is C_{1-12} alkyl, C_{7-10} phenylalkyl or a group of formula RCO-,

whereby

i) R is hydrogen, C_{1-11} alkyl, phenyl or C_{7-10} phenylalkyl, or

ii) RCO- is a) an L- or D-phenylalanine residue optionally ring-substituted by halogen and/or C_{1-3} alkyl,

b) H-Asn-, or

c) H-Nle-Asn-,

the α-amino group of amino acid residues a) and b) and the N-terminal amino group of dipeptide residues c) being optionally mono or di-C_{1-12} alkylated,

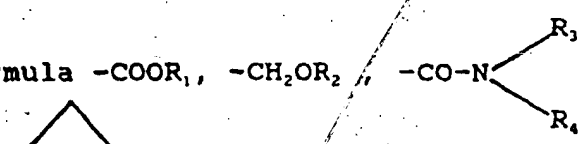
A′ is hydrogen or, when A is C_{1-12}alkyl or C_{7-10}phenylalkyl, also C_{1-12}alkyl or C_{7-10}phenylalkyl,

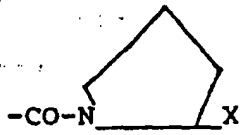
B is -Phe- optionally ring-substituted by halogen and/or C_{1-3}alkyl,

C is -(L)- or -(D)-Trp- optionally α-N-methylated and optionally benzene-ring-substituted by halogen and/or C_{1-3}alkyl,

D is -Lys- optionally α-N-methylated and optionally Σ-N-C_{1-3}-alkylated,

E is -Thr- or -Ala- each in (D)- or (L)-form and each being optionally α-N-methylated,

F is a group of formula $-COOR_1$, $-CH_2OR_2$,  or



wherein R_1 is hydrogen or C_{1-3}alkyl,

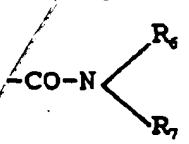
R_2 is hydrogen or the residue of a physiologically acceptable, physiologically hydrolysable ester,

R_3 is hydrogen, C_{1-3}alkyl, phenyl or C_{7-10}-phenylalkyl,

R_4 is hydrogen, C_{1-3}alkyl or, when R_3 is hydrogen or methyl, also a group of formula $-CH(R_5)-X$,

R_5 is hydrogen, $-(CH_2)_2-OH$, $-(CH_2)_3-OH$, $-CH_2-OH$, $-CH(CH_3)-OH$, isobutyl or benzyl

X is a group of formula $-COOR_1$, $-CH_2OR_2$ or



wherein

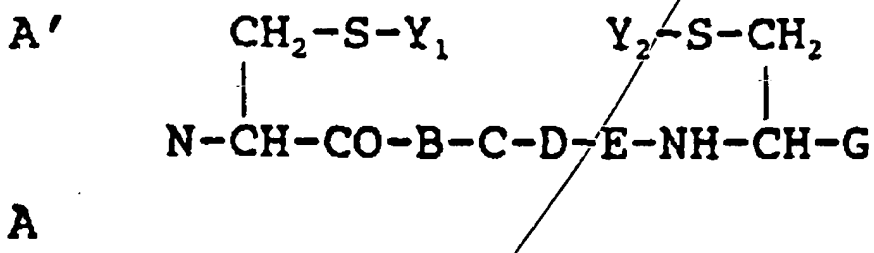
R_1 and R_2 have the meanings given above,

R_6 is hydrogen or C_{1-3}alkyl and

R_7 is hydrogen, C_{1-3}alkyl, phenyl or C_{7-10}phenylalkyl,

the group -CH(R,)-X having the D- or L- configuration, and Y, and Y, are each hydrogen or together represent a direct bond, whereby the residues in the I- and 6-position each independently have the L- or D-configuration.

92. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is a compound of formula



wherein

A is C_{1-12} alkyl, C_{7-10} phenylalkyl or a group of formula RCO-, whereby

i) R is hydrogen, C_{1-11} alkyl, phenyl or C_{7-10}.phenylalkyl or

ii) RCO- is

a) an L- or D-phenylalanine residue optionally r ing-substituted by F, Cl, Br, NO_2, NH_2, OH, C_{1-3} alkyl and/or C_{1-3} alkoxy;

b) the residue of a natural or synthetic α-amino acid other than defined under a) above or of a corresponding D-amino acid, or

C) a dipeptide residue in which the individual amino acid residues are the same or different and are selected from those defined under a) and/or b) above,

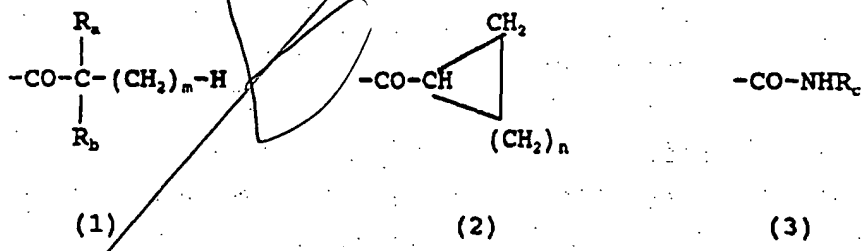
C_{1-8} alkanoyl,

A' is hydrogen,

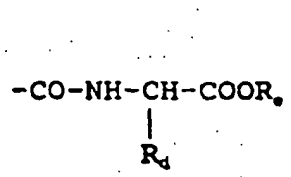
Y, and Y, represent together a direct bond or

each of Y, and Y, is independently hydrogen or a radical of formulae (1) to (5).

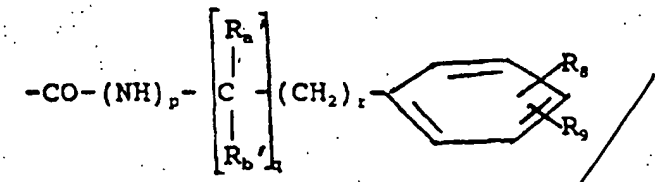
D2



(1) (2) (3)



(4)



(5)

wherein

R_a is methyl or ethyl

R_b is hydrogen, methyl or ethyl

m is a whole number from 1 to 4

n is a whole number from 1 to 5

R_c is (C_{1-6})alkyl

R_d represents the substituent attached to the α-carbon atom of a natural or synthetic α-amino acid (including hydrogen)

R_e is (C_{1-5})alkyl

R_a' and R_b' are independently hydrogen, methyl or ethyl,

R_8 and R_9 are independently hydrogen, halogen, (C_{1-3})alkyl or (C_{1-3})alkoxy,

P is 0 or 1,

q is 0 or 1, and

r is 0, 1 or 2,

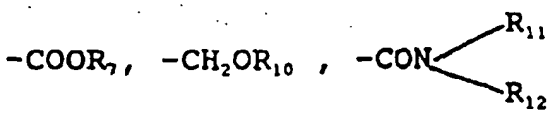
B is -Phe- optionally ring-substituted by halogen, NO_2, NH_2, OH, C_{1-3}alkyl and/or C_{1-3}alkoxy (including pentafluoroalanine), or ß-naphthyl-Ala

C is (L)-Trp- or (d)-Trp- optionally α-N-methylated and optionally benzene-ring-substituted by halogen, NO_2, NH_2 OH, C_{1-3}alkyl and/or C_{1-3} alkoxy,

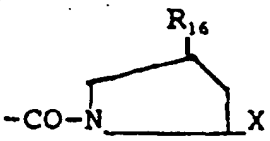
D is Lys, Lys in which the side chain contains O or S in ß-position, F-Lys or δF-Lys, optionally α-N-methylated, or a 4-aminocyclohexylAla or 4-aminocyclohexylGly residue

E is The, Ser, Val, Phe, Ile or an aminoisobutyric or aminobutyric acid residue

G is a group of formula



or



wherein

R_7 is hydrogen or C_{1-3}alkyl,

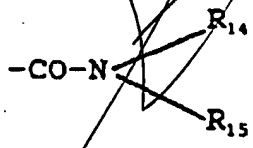
R_{10} is hydrogen or the residue of a physiologically acceptable, physiologically hydrolysable ester,

R_{11} is hydrogen, C_{1-9}alkyl, phenyl or C_{7-10}phenyl-alkyl,

R_{12} is hydrogen, C_{1-3}alkyl or a group of formula $-CH(R_{13})-X_1$,

R_{13} is CH_2OH, $-(CH_2)_2-OH$, $-(CH_2)_3-OH$, or $-CH(CH_3)OH$ or represents the substituent attached to the α-carbon atom of a natural or synthetic α-amino acid (including hydrogen) and

X_1 is a group of formula $-COOR_7$, $-CH_2OR_{10}$ or



wherein

R_7 and R_{10} have the meanings given above,

R_{14} is hydrogen or C_{1-3}alkyl and

R_{15} is hydrogen, C_{1-3}alkyl, phenyl or C_{7-10}phenylalkyl, and

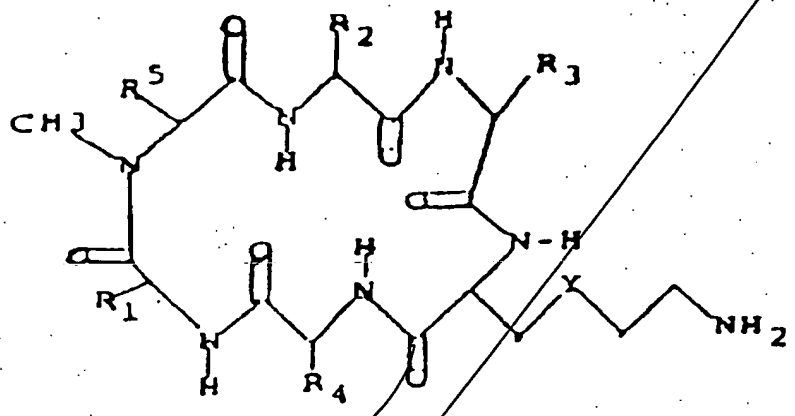
R_{16} is hydrogen or hydroxy,

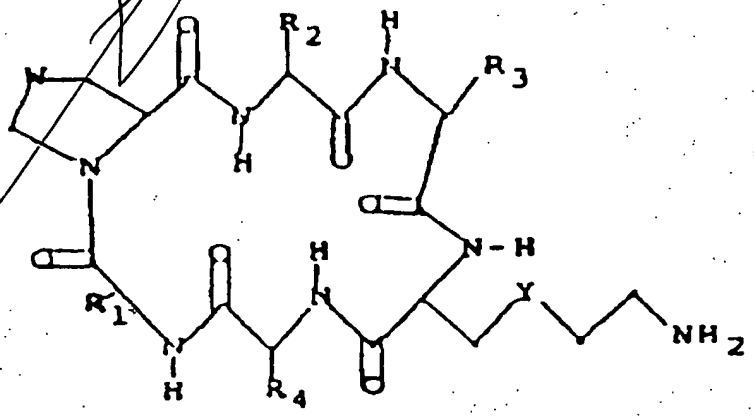
with the proviso that

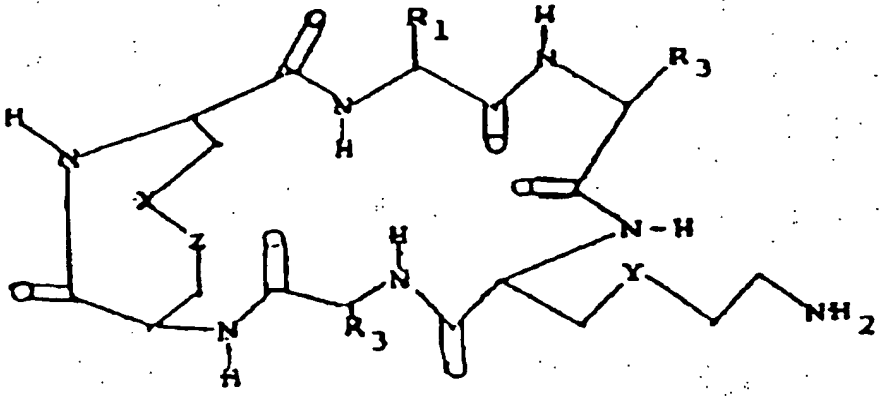
when R_{12} is $-CH(R_{13})-X_1$ then R_{11} is hydrogen or methyl,

wherein the residues B, D and E have the L-configurati n, and the residues in the 2-and 7-position and any r sidues Y_1 4) and Y_2 4) each independently have the (L)- or (D)- configuration.

93. A pharmaceutical composition according to Claim 59, wherein the analog is a somatostatin analog selected from the compounds of the following formulae





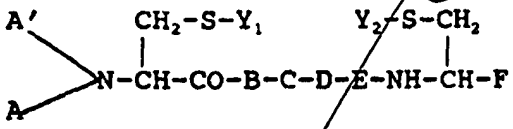


wherein

W is	S or $(CH_2)_s$ where s is 0, 1 or 2;
one of X and Z	is S and the other is S or CH_2;
Y is	S or $(CH_2)_t$ where t is 0, 1 or 2;
each of R_1 and R_2	independently of the other, is C_{1-5} alkyl, benzyl, benzyl having one or two C_{1-5} alkyl, halogen, hydroxy, amino, nitro, and/or C_{1-5} alkoxy substituents, or C_{1-5} alkyl substituted with 5- or 6-membered heterocyclic ring;
R_3 is	3-indolymethyl, either unsubstituted or having C_{1-5} alkyl, C_{1-5} alkoxy or halogen substitution;
R_4	C_{1-5} alkyl, C_{1-5} hydroxyalkyl, benzyl, carboxy-(C_{1-5} alkyl), amino (C_{1-5} alkyl) or benzyl having a C_{1-5} alkyl, halogen, hydroxy, amino, nitro and/or C_{1-5} alkoxy substituent;
R_5 is	C_{1-5} alkyl, benzyl, or benzyl having a C_{1-5} alkyl, halogen, hydroxy, amino, nitro, and/or C_{1-5} alkoxy substituent,

D2

compounds of formula



wherein

A is C_{1-12} alkyl, C_{7-10} phenylalkyl or a group of formula RCO-, whereby

i) R is hydrogen, C_{1-11} alkyl, phenyl or C_{7-10} phenylalkyl, or

ii) RCO- is

a) an L- or D-phenylalanine residue optionally ring-substituted by F, Cl, Br, NO_2, NH_2, OH, C_{1-3} alkyl and/or C_{1-3} alkoxy

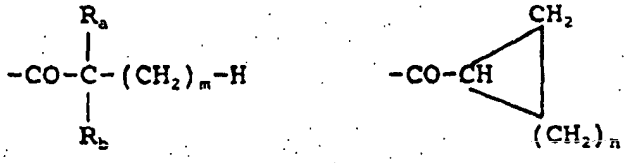
b) the residue of a natural α-amino acid other than defined under a) above r of a corresponding D-amino acid, or

c) a dipeptide residue in which the individual amino acid

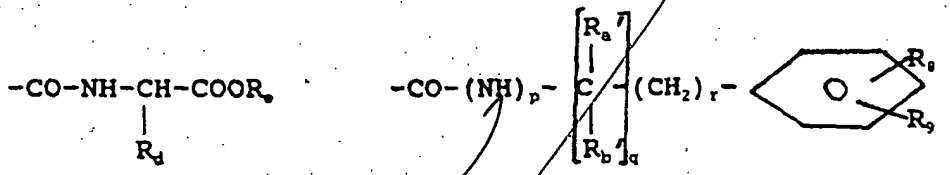
residues are the same or different and are selected from those defined under a) and/or b) above, the α-amino group or amino acid residues a) and b) and the N-terminal amino group of dipeptide residues c) being optionally mono- or di-C_{1-12} alkylated,

A' is hydrogen or, when A is C_{1-12} alkyl or C_{7-10} phenylalk- also C_{1-12} alkyl or C_{7-10} phenylalkyl,

Y_1 and Y_2 represent together a direct bond or each of Y_1 and Y_2 is independently hydrogen or a radical of the formulae



(1) (2) (3)



(4) (5)

wherein R_a is methyl or ethyl

R_b is hydrogen, methyl or ethyl

m is a whole number from 1 to 4

n is a whole number from 1 to 5

R_c is (C_{1-6})alkyl

R_d represents the substituent attached to the α-carbon atom of a natural α-amino acid (including hydrogen)

R_e is (C_{1-5})alkyl

R_a' and R_b' are independently hydrogen, methyl or ethyl,

R_8 and R_9 are independently hydrogen, halogen, (C_{1-3})alkyl or (C_{1-3})alkoxy,

p is 0 or 1,

q is 0 or 1, and

r is 0, 1 or 2,

B is -Phe- optionally ring-substituted by halogen, No_2, NH_2,

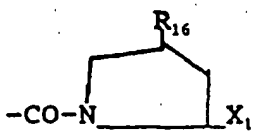
OH, C_{1-3}alkyl and/or C_{1-3}alkoxy, or naphthylalanine.

C is (L)-Trp- or (D)-Trp- optionally α-N-methylated and optionally benzene-ring-substituted by halogen, No_2, NH_2, OH, C_{1-3} alkyl and/or C_{1-3} alkoxy,

D is -Lys-, ThiaLys, F-Lys, δF-Lys or Orn, optionally α-N-methylated, or a 4-aminocyclohexyl Ala or 4-aminocyclohexyl Gly residue,

E is Thr, Ser, Val, Phe, Ile or an aminoisobutyric acid residue

F is a group of formula $-COOR_7$, $-CH_2OR_{10}$, $-CON(R_{11})(R_{12})$ or



wherein R_7 is hydrogen or C_{1-3}alkyl,

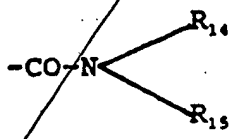
R_{10} is hydrogen or the residue of a physiologically acceptable, physiologically hydrolysable ester,

R_{11} is hydrogen, C_{1-3}alkyl, phenyl or C_{7-10}-phenylalkyl,

R_{12} is hydrogen, C_{1-3}alkyl or a group of formula $-CH(R_{13})-X_1$,

R_{13} is CH_2OH, $-(CH_2)_2-OH$, $-(CH_2)_3-OH$, or $-CH(CH_3)OH$ or represents the substituent attached to the α-carbon atom of anatural α-amino acid (including hydrogen) and

X_1 is a group of formula $-COOR_7$, $-CH_2OR_{10}$ or



wherein

R_7 and R_{10} have the meanings given above,

R_{14} is hydrogen or C_{1-3}alkyl and

R_{15} is hydrogen, C_{1-3}alkyl, phenyl or C_{7-10}phenylalkyl, and

R_{16} is hydrogen or hydroxy,

with the proviso that

when R_{12} is $-CH(R_{13})-X_1$ then R_{11} is hydrogen or methyl,

wherein the residues B, D and E have th L-configuration, and the residues in the 2- and 7-position and any residues Y_1 4) and Y_2 4) each independently have the (L)- or (D)-configuration and compounds of the following formulae

H-Cys-Phe-(D)Trp-Lys-Thr-Phe-Cys-OH

-Asn-Phe-Phe-(D)Trp-Lys-Thr-Phe-Gaba-

-MeAla-Tyr-(D)Trp-Lys-Val-Ph

NMe-Phe-His-(D)Trp-Lys-Val-Ala.

94. A pharmaceutical composition according to Claim 59, wherein the analogs are Somatostatin analogs

X-Cys-D-o-Trp-E-F-Cys-Y I [SEQ ID 4]

X-Cys-Lys-Asn-Phe-D-o-Trp-E-F-Phe-Thr-Ser-Cys-Y II [SEQ ID 5]

I,II, X = N-terminus anchor; Y = C-terminus anchor, G-I or its alc; wherein at least I of X, Y = cationic anchor; D = Phe Tyr, 3-(p-fluorophenyl)alanine or 3 (p-chlorophenyl)alanine residue; E = Lys, Lys(R^1); R^1 = C_{1-8}(fluoro)alkyl; F = Thr, Val, Ser; G = D- or L-Thr, Phe, or 3-(2-naphthyl)alanine residue; I = OH, NH_2, NHR^1.

95. A pharmaceutical composition according to Claim 59, wherein the somatostatin analogs are peptides:

$RR^1NCHR^2CONHCH(CH_2SR^4)CO$-Phe-Trp-Lys-X-$NHCHRCH_2SR^5$

[R inorg. or org. acyl group, R^1 = H, alkyl, $NCHR^2CO$ moiety = I.

$Me(CH_2)_8CO$-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-ol I

or D-Phe (optionally ring substituted by halo, NO_2, OH, alkyl. alkoxy); Phe, Trp, (D or L) ,may be ring substituted by NO_2, NH_2, OH, alkyl, alkoxy; Lys may be α-N-methylated and Σ-N-alkylated; X = D- or L-α-amino acid residue optionally α-N-methylated; R^3 = CO_2H, CH_2OH, carbamoyl, R^4 = R^5 = H, R^4R^5 = bond]

96. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

H-Ser-Ala-Asn-Ser-Asn-Pro-Ala-X-Ala-Pro-Arg-Glu-Arg-Lys-Ala-Gly

Cys-X^1-X^2-Phe-Phe-D-Trp-Lys-Tys-Thr-X^3-X^4-X^5-X^6-OH

97. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

H-Ser-Ala-Asn-Ser-Asn-Pro-Ala-Leu-Ala-Pro-Arg-Glu-Arg-Lys-Ala-Gly-

Cys-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Tyr-Thr-Ser-Cys-OH

98. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is

c(Spacer-Phe-D-Trp-Lys-Thr)

Spacer may stand for:

a) R,S-δ-Bn-o-AMPA

b) R-α-Bn-Me-o-AMPA

c) Phe-Pro

99. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

H_2N-Ala-Gly-Cys-Lys-Asn-Phe-Phe-Trp-Lys-Thr-Phe-Thr-Ser-Cys-OH [SEQ ID NO 6]

100. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

H_2N-Ser-Ala-Asn-Ser-Asn-Pro-Ala-Met-Ala-Pro-Arg-Glu-Arg-Lys-Ala-Gly-Cys-Lys-Asn-Phe-Phe-Trp-Lys-Thr-Phe-Thr-Ser-Cys-OH [SEQ ID No 7]

101. A pharmaceutical composition according to Claim 59,

wherein the somatostatim analog is:

D-β-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2

102. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

Ac-Phe -Cys -Phe-D -Trp -Lys -Thr -Cys -Thr-NH_2

103. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Trp-NH_2

D2

104. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Trp-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH_2

105. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2

106. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Trp-NH_2

107. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

3-(2-naphthyl)-D-Ala-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH_2

108. A pharmaceutical composition according to Claim 59, wherein the somatostatin analog is:

c(Aha-Phe-p-Cl-Phe-D-Trp-Lys-Thr-Phe)

Aha = 7 -amino heptanoic acid.

109. A pharmaceutical composition according to Claim 59, wherein the active ingredient is diazoxide and comprises in addition a thiazide selected among chlorothiazide, hydrochlorothiazide, trichloromethiazide and polythiazide.

110. A method for the treatment of symptoms of syndrome X by administering to a patient a pharmaceutical composition according to Claim 59 comprising a pharmaceutically effective dosage of a compound selected among somatostatin or one of its analogs, diazoxide or one of its analogs, cyclothiazideor one of its analogsand metformin.

111. A method according to Claim 110, wherein the pharmaceutically effective dosage (calculated on octreotide) does not exceed 50μ/kg/day.

112. A method according to Claim 110, wherein said dosage does not exceed 40μ/kg/day.

113. A method according to Claims 109 wherein the analog is Octreotide which is applied in the form of an injection in a 0.9% saline solution.

114. A method according to Claim 109, wherein said dosage does not exceed 8 mg/kg/day in the treatment of the active ingredient (calculated on diazoxide) in adults, and does not exceed 15/mg/day in the treatment of children.

115. A method according to Claim 109, wherein the amount of metformin applied does not exceed 2.5 g/day divided into 2 -3 portions.

116. The method of formulating a composition containing a compound selected among somatostatin or one of its analogs, diazoxide or one of its analogs, cyclothiazide or one of its analogs and metformin in a preparation for the treatment of the risk factors of syndrome X of Reaven.